

SUPPLEMENTAL MATERIAL

TITLE:

Endocrine Profiling and Prioritization of Environmental Chemicals Using ToxCast Data

AUTHORS:

David Reif^{1*}, Matthew Martin¹, Shirlee Tan², Keith Houck¹, Richard Judson¹, Ann Richard¹, Thomas Knudsen¹, David Dix¹, Robert Kavlock¹

AUTHOR AFFILIATIONS:

¹National Center for Computational Toxicology

Office of Research and Development

US Environmental Protection Agency

Research Triangle Park, NC

²Office of Science Coordination and Policy

Office of Pollution Prevention, Pesticides and Toxic Substances

US Environmental Protection Agency

Washington, DC

*CONTACT INFORMATION FOR CORRESPONDING AUTHOR:

Name: David Reif

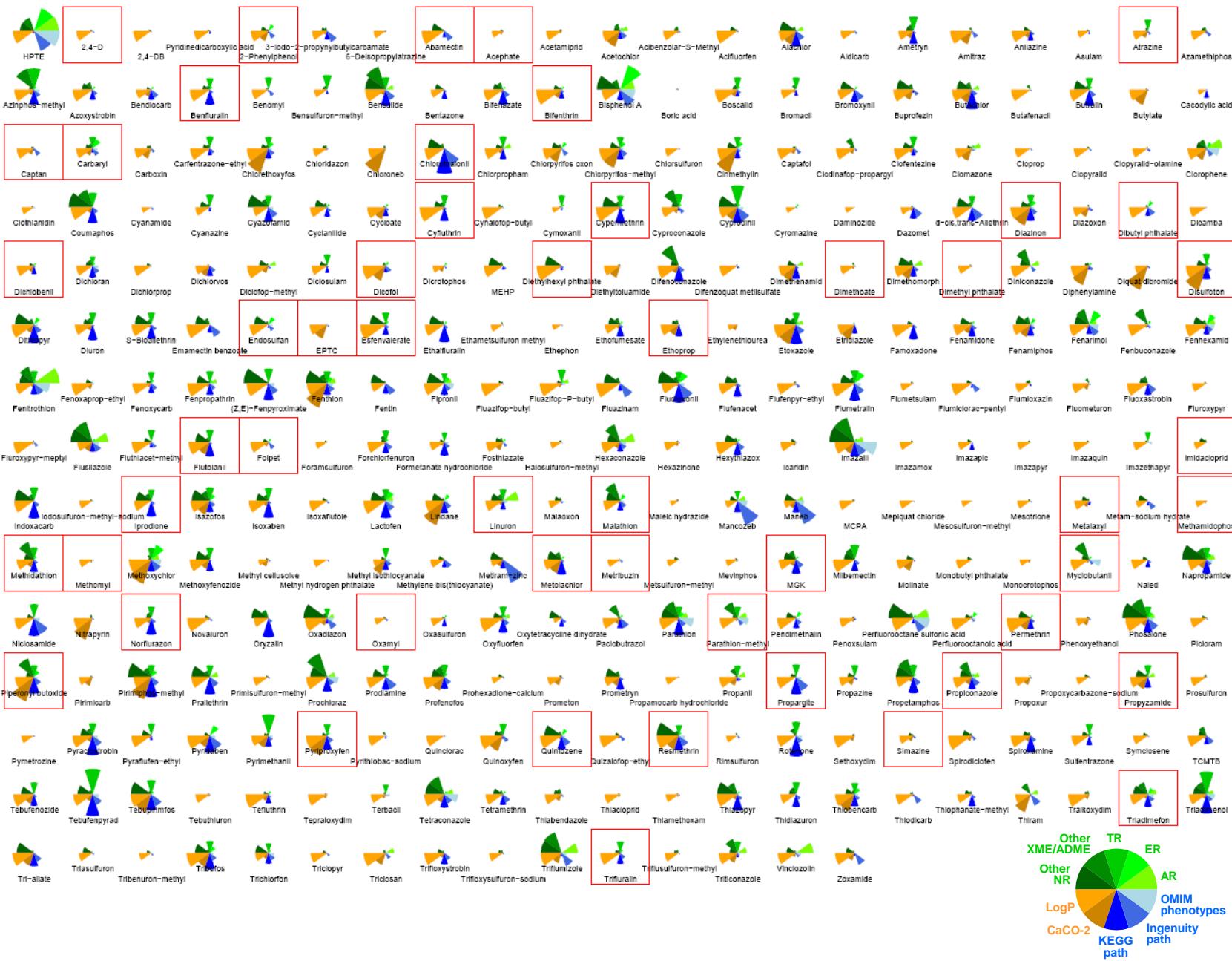
Email: reif.david@epa.gov

Phone: 919-541-2574

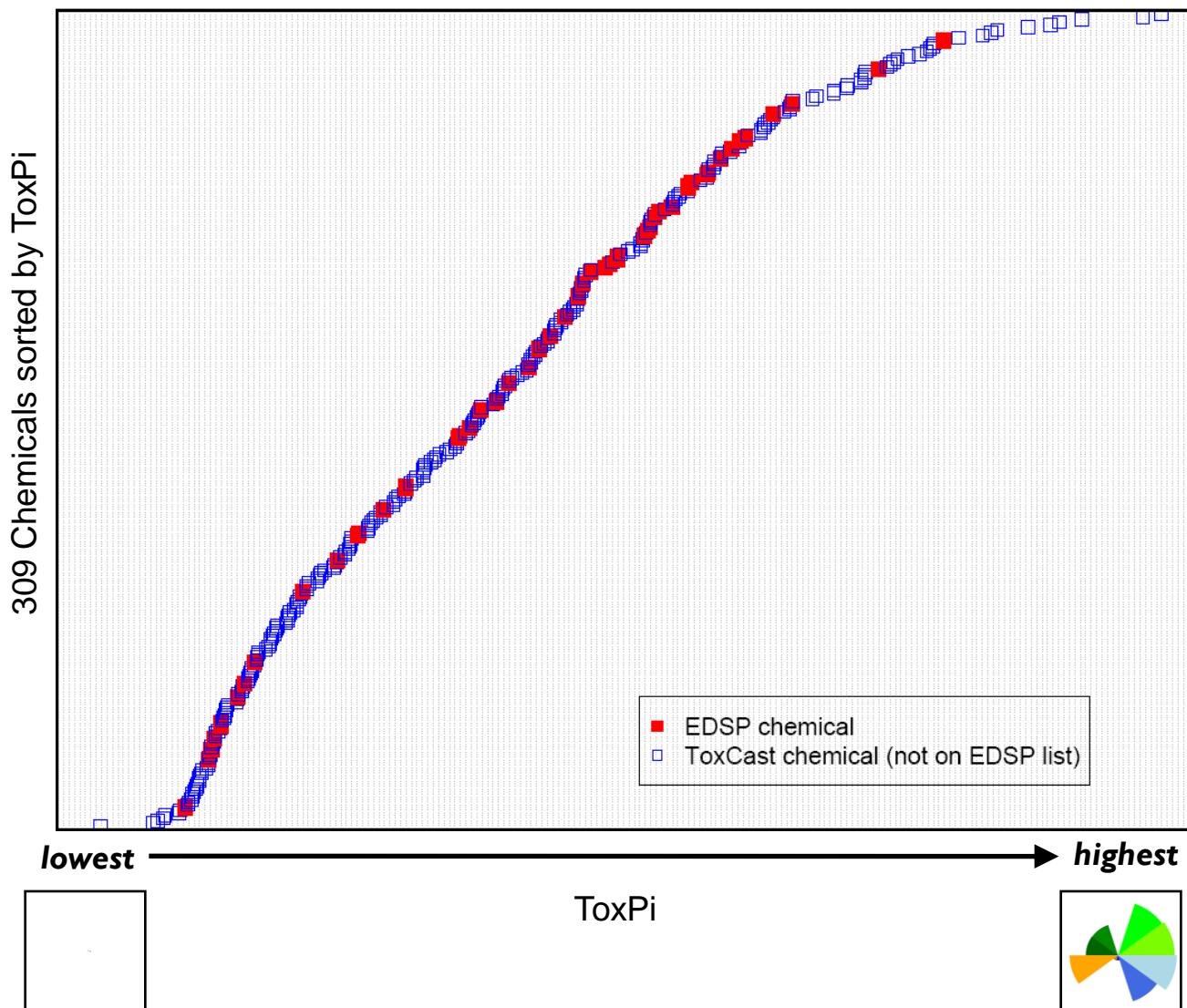
Fax: 919-541-1194

Address: Mail Drop B-205-01, US EPA, Research Triangle Park, NC, 27711

Supplemental Material, Figure 1: ToxPi profiles for all 309 ToxCast Phase I chemicals. The profiles are arranged in alphabetical order by chemical name (although abbreviations may be written on the figure for clarity). The EDSP chemicals are highlighted by solid red frames.



Supplemental Material, Figure 2: Initial EDSP Tier 1 chemicals highlighted along the sorted ToxPi distribution for all 309 ToxCast Phase I chemicals. The ToxPi (horizontal axis) for each chemical (vertical axis) is symbolized by a blue box, sorted according to overall ToxPi. The EDSP chemicals are highlighted by solid red boxes.



Supplemental Material, Figure 3: : ToxPi profiles for all Triazole fungicides in ToxCast Phase I.



Cyproconazole



Difenoconazole



Diniconazole



Fenbuconazole



Flusilazole



Hexaconazole



Myclobutanil



Propiconazole



Tetraconazole



Triadimefon



Triadimenol



Triticonazole

Supplemental Material, Table 1: List of components making up each slice. The names given here are the ToxMiner IDs, for which full descriptions are available in (Judson RS et al., *Environ Health Perspect*, 2010). Links to all data tied to particular ToxMiner IDs are also available at (<http://www.epa.gov/ncct/toxcast/>) and in Supplemental Table 2.

IN VITRO ASSAYS

AR (5)

"ATG_AR_TRANS" "NCGC_AR_Agonist" "NVS_NR_rAR" "NVS_NR_hAR" "NCGC_AR_Antagonist"

ER (6)

"NVS_NR_hER" "NVS_NR_bER" "NCGC_ERalpha_Agonist" "ATG_ERa_TRANS" "ATG_ERE_CIS"
"NCGC_ERalpha_Antagonist"

TR (5)

"NCGC_TRbeta_Agonist" "ATG_THRa1_TRANS" "NVS_NR_hTRa" "CLZD_UGT1A1_48" "NCGC_TRbeta_Antagonist"

XME/ADME (38)

"NVS_ADME_hCYP19A1"	"CLZD_CYP1A1_48"	"CLZD_CYP1A2_48"	"CLZD_CYP2B6_48"	"CLZD_CYP3A4_48"
"NVS_ADME_hCYP1A1"				
"NVS_ADME_hCYP1A2"	"NVS_ADME_hCYP1B1"	"NVS_ADME_hCYP2A6"	"NVS_ADME_hCYP2B6"	
"NVS_ADME_hCYP2C18"	"NVS_ADME_hCYP2C19"			
"NVS_ADME_hCYP2C19_Activator"	"NVS_ADME_hCYP2C8"	"NVS_ADME_hCYP2C9"	"NVS_ADME_hCYP2D6"	
"NVS_ADME_hCYP2E1"	"NVS_ADME_hCYP2J2"			
"NVS_ADME_hCYP3A4"	"NVS_ADME_hCYP3A5"	"NVS_ADME_hCYP4F12"	"NVS_ADME_hCYP4F12_Activator"	
"NVS_ADME_rCYP1A1"	"NVS_ADME_rCYP1A2"			
"NVS_ADME_rCYP2A1"	"NVS_ADME_rCYP2A2"	"NVS_ADME_rCYP2B1"	"NVS_ADME_rCYP2C11"	
"NVS_ADME_rCYP2C12"	"NVS_ADME_rCYP2C13"			
"NVS_ADME_rCYP2C6"	"NVS_ADME_rCYP2D1"	"NVS_ADME_rCYP2D2"	"NVS_ADME_rCYP2E1"	
"NVS_ADME_rCYP3A1"	"NVS_ADME_rCYP3A2"			
"CLZD_SULT2A1_48"	"CLZD_HMGCS2_48"			

Other NR (36)

"ATG_Ahr_CIS"	"ATG_CAR_TRANS"	"ATG_ERRa_TRANS"	"ATG_ERRg_TRANS"	"ATG_FXR_TRANS"
"ATG_GR_TRANS"	"ATG_GRE_CIS"			
"ATG_LXRa_TRANS"	"ATG_LXRb_TRANS"	"ATG_PPARa_TRANS"	"ATG_PPARd_TRANS"	"ATG_PPARg_TRANS"
"ATG_PXR_TRANS"	"ATG_PXRE_CIS"			
"ATG_RARa_TRANS"	"ATG_RARB_TRANS"	"ATG_RARg_TRANS"	"ATG_RXRa_TRANS"	"ATG_RXRb_TRANS"
"NCGC_LXR_Agonist"	"NCGC_PPARg_Agonist"			
"NCGC_PXR_Agonist_human"	"NCGC_PXR_Agonist_rat"	"NCGC_RXRa_Agonist"	"NVS_NR_bPR"	"NVS_NR_hCAR"
"NVS_NR_hCAR_Agonist"	"NVS_NR_hFXR"			
"NVS_NR_hGR"	"NVS_NR_hPPARa"	"NVS_NR_hPPARg"	"NVS_NR_hPR"	"NVS_NR_hPXR"
"NVS_NR_hRAR"	"NCGC_PPARa_Agonist"			
"NCGC_PPARd_Agonist"				

CHEMICAL PROPERTIES

LogP (1)

"LogP"

Predicted Caco-2 (1)

"PCaco_QP"

PATHWAYS

KEGG "Perturbation Score" Pathways (12)

"PS_KEGG_Adipocytokine_signaling_pathway" "PS_KEGG_Androgen_and_estrogen_metabolism"
"PS_KEGG_Androgen_and_estrogen_metabolism_Mus_musculus"
"PS_KEGG_Biosynthesis_of_steroids" "PS_KEGG_Biosynthesis_of_steroids_Mus_musculus"
"PS_KEGG_GnRH_signaling_pathway"
"PS_KEGG_GnRH_signaling_pathway_Rattus_norvegicus" "PS_KEGG_Insulin_signaling_pathway" "PS_KEGG_Melanogenesis"
"PS_KEGG_Melanogenesis_Rattus_norvegicus" "PS_KEGG_PPAR_signaling_pathway" "PS_KEGG_Thyroid_cancer"

Ingenuity "Perturbation Score" Pathways (8)

"PS_Ingenuity_Aryl_Hydrocarbon_Receptor_Signaling" "PS_Ingenuity_Estrogen_Receptor_Signaling"
"PS_Ingenuity_Glucocorticoid_Receptor_Signaling"
"PS_Ingenuity_Insulin_Receptor_Signaling" "PS_Ingenuity_PPARaRXRa_Activation" "PS_Ingenuity_PPAR_Signaling"
"PS_Ingenuity_RAR_Activation" "PS_Ingenuity_TRXR_Activation"

OMIM "Perturbation Score" Phenotypes (7)

"PS_Phenotype_OMIM_Agammaglobulinemia_and_isolated_hormone_deficiency_307200_3"
"PS_Phenotype_OMIM_Androgen_insensitivity_300068_3"
"PS_Phenotype_OMIM_Aromatase_deficiency_3" "PS_Phenotype_OMIM_Estrogen_resistance_3"
"PS_Phenotype_OMIM_Progesterone_resistance_264080_2" "PS_Phenotype_OMIM_Thyroid_hormone_resistance_188570_3"
"PS_Phenotype_OMIM_Pituitary_adenoma_nonfunctioning_3"